Supplementary Material

An efficient and scalable synthesis of thiazolo ring fused 2-pyridones using flow chemistry

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C10 from flow synthesis:

\[ ^{1}H\ NMR: \]

\[ ^{13}C\ NMR: \]
Chiral HPLC traces:

Chiral HPLC of cyclopropyl thiazoline 11 was carried out using a Diacel Chiracel OD-H (250 x 4.6 mm) column and eluting isocratically (Hexane:PrOH 90:10) at ambient temperature, then detected by UV at 254 nm. Injection was 10 μL at 1 mg/mL in CHCl₃. Chiral HPLC of pyridone 13 was carried out using a Lux 5 μm i-amyllose-1 (250 x 4.6 mm) column and eluting on a gradient (PrOH 30:70 to 100% hexane) at ambient temperature, then detected by UV at 254 nm. Injection was 10 μL at 1 mg/mL in MeOH.

Thiazoline (pure):

Supporting Figure 1. Chiral HPLC trace of thiazoline 12, as used for MWI and flow syntheses. ee of the mixture = 100%, [α]D +83° (c 0.5, CHCl₃)
Thiazoline (epimerized):

Supporting Figure 2. Thiazoline 12 post-epimerization, demonstrating that R and S forms can be distinguished. ee of the mixture = 52%, [α]₀ +44° (c 0.5, CHCl₃).
Thiazoline (mixture of enantiopure and epimerized thiazoline):

Supporting Figure 3. Mixture of pure and epimerised thiazoline 12 confirms the identity of the peaks. ee of the mixture = 74% (c 0.5, CHCl₃).
2-Pyridone 13 (Prepared using MWI conditions):

Supporting Figure 4. Enantiopurity of pyridone 13, as synthesised by MWI. ee of the mixture = 82%, $[\alpha]_D^{-188^\circ}$ (c 0.5, CHCl$_3$).
2-Pyridone 13 (Prepared under flow conditions):

Supporting Figure 5. Enantiopurity of pyridone 13, as synthesised by flow. ee of the mixture = 73%, [α]D -146° (c 0.5, CHCl₃).
Supporting Figure 6. Blank Injection of MeOH to account for the HPLC baseline.